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A mechanism of lyso-Gb3-induced podocyte injury

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Objectives: Fabry disease is an X-linked lysosomal glycosphingolipid storage disorder resulting in the deficiency of the α-galactosidase A enzyme, eventually leading to end-stage renal disease. Podocyte injury is the one of early characteristic phenotype of Fabry nephropathy. Globotriaosylsphingosine (lyso-Gb3) is a bioactive molecule that accumulates in Fabry disease. However, the association between molecular mechanisms of lyso-Gb3 and renal damage is not well known. Thus, we investigated a mechanism how lyso-Gb3 induced podocyte injury.

Methods: We used immortalized mouse podocytes for in vitro experiments. Lyso-Gb3 (100μM, 200μM) was used to induce Fabry disease mimic condition. The effect of lyso-Gb3 on podocyte injury was evaluated by western blot, immunofluorescence, and albumin permeability analysis.

Results: Fibronectin, which is fibrosis marker, was increased in dose-dependent manner by treatment with lyso-Gb3. Synaptopodin was decreased and receptor interacting serine/threonin kinase 3 (RIPK3) was increased after lyso-Gb3 treatment. A rearrangement of F-actin switched from the center to cell periphery by lyso-Gb3 treatment was observed compared to controls. Also increased albumin permeability was observed in lyso-Gb3-treated podocytes.

Conclusions: These results suggest that lyso-Gb3 may induce albuminuria caused by podocyte injury due to rearrangement of F-actin.

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